

AMENDMENTS TO THE CLAIMS

Claim identifiers have been changed in this listing of the claims as compared to the response filed on January 29, 2009. No new claims or claim amendments are entered as compared to the earlier filed response.

Claims 1-48 (Canceled).

49. (Currently amended) A method for treating ischemic myocardial tissue of a mammal in need of such treatment comprising:

a) identifying a mammal which has, is suspected of having, or will have the ischemic tissue;

b) injecting an effective amount of a solution comprising a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue; and

c) administering to the mammal an effective amount of granulocyte macrophage colony stimulating factor (GM-CSF) or an effective fragment thereof, thereby treating the ischemic myocardial tissue of the mammal, wherein the GM-CSF or an effective fragment thereof is administered systemically.

50. (Previously presented) The method of claim 49, wherein the angiogenic protein is a vascular endothelial growth factor (VEGF) or an effective fragment thereof.

51. (Previously presented) The method of claim 50, wherein the VEGF is VEGF-1, VEGF-2, or VEGF165.

52. (Previously presented) The method of claim 49, further comprising expressing the angiogenic protein or fragment in the myocardium.

53. (Previously presented) The method of claim 52, wherein the method further comprises increasing frequency of endothelial progenitor cells (EPC) in the mammal.

54. (Previously presented) The method of claim 52, wherein the increase in frequency of the EPC is at least about 20% as determined by a standard EPC isolation assay.

55. (Previously presented) The method of claim 52, wherein the method further comprises increasing EPC differentiation in the mammal.

56. (Previously presented) The method of claim 55, wherein the increase in EPC differentiation is at least about 20% as determined by a standard EPC culture assay or a standard hindlimb ischemia assay.
57. (Previously presented) The method of claim 50, wherein the level of VEGF or VEGF fragment expression is sufficient to increase neovascularization by at least about 5% as determined by a standard cornea micropocket assay.
58. (Previously presented) The method of claim 49, wherein the amount of administered GM-CSF or fragment thereof is sufficient to increase bone marrow-derived EPC incorporation into foci.
59. (Previously presented) The method of claim 58, wherein the increase in-bone marrow-derived EPC incorporation into foci is at least about 20% as determined by a standard rodent bone marrow (BM) transplantation model.
60. (Previously presented) The method of claim 49, wherein the method further comprises administering at least one angiogenic protein or effective fragment thereof before or after administration of the nucleic acid to the mammal.
61. (Previously presented) The method of claim 49, wherein the method further comprises administering to the mammal one or more of urokinase, plasminogen activator, and heparin.
62. (Canceled)
63. (Previously presented) The method of claim 49, wherein the nucleic acid is directly injected with a catheter or stent.
64. (Previously presented) The method of claim 49, wherein the nucleic acid is inserted into a cassette operably linked to a promoter.
65. (Previously presented) The method of claim 49, wherein the myocardial tissue is ischemic or is associated with infarction or dysfunction.
66. (Previously presented) The method of claim 49, wherein the angiogenic protein or fragment thereof is one of acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TGF- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor

(IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF), granulocyte/macrophage CSF (GM-CSF), stem cell factor (SCF), angiopoietin-1 (Ang1), nitric oxide synthase (NOS); or a mutein thereof.

67. (Canceled)

68. (Currently amended) A method for treating ischemic myocardial tissue of a mammal in need of such treatment comprising:

a) administering to the mammal an effective amount of granulocyte macrophage colony stimulating factor (GM-CSF) or an effective fragment thereof, wherein the GM-CSF or an effective fragment thereof is administered systemically; and

b) administering an effective amount of a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue; thereby treating the ischemic myocardial tissue of the mammal. .

69. (Currently amended) A method for treating ischemic myocardial tissue of a mammal in need of such treatment comprising:

a) administering to a mammal an effective amount of a cytokine that mobilizes endothelial progenitor cells, wherein the cytokine or an effective fragment thereof is administered systemically; and

b) subsequently administering an effective amount of a nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue, wherein the method increases the neovascularization of said tissue thereby treating the ischemic myocardial tissue of the mammal. .

70. (Previously presented) The method of claim 69, wherein the cytokine is GM-CSF.

71. (Canceled)

72. (Previously presented) The method of claim 68, wherein the angiogenic protein or fragment thereof is one of acidic fibroblast growth factor (aFGF), basic fibroblast growth factor (bFGF), epidermal growth factor (EGF), transforming growth factor α and β (TGF- α and TGF- β), platelet-derived endothelial growth factor (PD-ECGF), platelet-derived growth factor (PDGF), tumor necrosis factor α (TNF- α), hepatocyte growth factor (HGF), insulin like growth factor (IGF), erythropoietin, colony stimulating factor (CSF), macrophage-CSF (M-CSF),

granulocyte/macrophage CSF (GM-CSF), stem cell factor (SCF), angiopoietin-1 (Ang1), nitric oxide synthase (NOS); or a mutein thereof.

73-75. (Cancelled)

76. (New) The method of claim 49, comprising an increase in neovascularization from 50% to 300% in the ischemic tissue.

77. (New) The method of claim 68, comprising an increase in neovascularization from 50% to 300% in the ischemic tissue.

78. (New) The method of claim 69, comprising an increase in neovascularization from 50% to 300% in the ischemic tissue.

79. (New) The method of claim 49, wherein the administration of GM-CSF or an effective fragment thereof comprises administration of the GM-CSF one week prior to administration of the nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue.

80. (New) The method of claim 68, wherein the administration of GM-CSF or an effective fragment thereof comprises administration of the GM-CSF one week prior to administration of the nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue.

81. (New) The method of claim 69, wherein the cytokine or an effective fragment thereof comprises administration of the cytokine one week prior to administration of the nucleic acid encoding at least one angiogenic protein or an effective fragment thereof into the myocardial tissue.